The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board

Paper No. 25

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte M. DAVID GOLDENBERG

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Appeal No. 1997-2368
Application 08/158,782

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HEARD: November 16, 2000

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Before ROBINSON, SPIEGEL, and SCHEINER, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1, 3-6, 8-10, 19, 20, 24, 25, 39-44, and 46-48. Claims 13-18, 21-23, 38, and 45 stand withdrawn by the examiner as directed to non-elected subject matter and are not before us in this appeal.

Claim 1 is illustrative of the subject matter on appeal and reads as follows:

1. A method of targeting a therapeutic agent to a focus of infection, which comprises parenterally injecting a patient infected with a pathogen with an effective amount of a polyspecific antibody-therapeutic agent conjugate;

wherein said conjugate comprises an immunoreactive composite of a plurality of chemically-linked antibodies or antibody fragments which specifically binds to a plurality of accessible epitopes on a single species of pathogen or of an antigen shed by said pathogen or resulting from the fragmentation or destruction of said pathogen and which is accreted at said focus of infection,

wherein said polyspecific antibody conjugate further comprises a chemically bound therapeutic agent for treating said infection.

The references relied upon by the examiner are:

Rodwell et al. (Rodwell)	4,671,958	June 9, 1987
Goldenberg ('525)	5,120,525	June 9, 1992
Goldenberg ('567)	5,332,567	July 26, 1994

Holder et al. (Holder), “Biosynthesis and Processing of a Plasmodium Falciparum Schizont Antigen Recognized by Immune Serum and a Monoclonal Antibody,” J. Exp. Med., Vol. 156, pp. 1528-538 (Nov. 1982)

Brennan et al. (Brennan), "Preparation of Bispecific Antibodies by Chemical Recombination of Monoclonal Immunoglobulin G_1 Fragments,” Science, Vol. 229, pp. 81-83 (July 1985)

GROUNDS OF RECORD

Claims 1, 3-6, 8-10, 19, 20, 24, 25, 39-44, and 46-48 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Rodwell, Holder, Goldenberg ('525), and Brennan.

Claims 1, 3-6, 8-10, 19, 20, 24, 25, 39-44, and 46-48 stand rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1-29 of U.S. Patent 5,332,567 to Goldenberg.

We reverse.

BACKGROUND

The invention is described by applicants, at pages 4 and 8 of the specification, as being directed to a method of targeting a therapeutic agent to a focus of infection which comprises injecting an infected patient with an antibody conjugate, the antibodies of which specifically bind to accessible epitopes of a pathogen associated with the infection or a pathogen-associated antigen, wherein the conjugate is comprised of a plurality of chemically linked antibodies or fragments thereof and a chemically linked therapeutic agent. The use of the conjugate in the manner claimed is stated to result in an increased likelihood that the therapeutic agent will reach the site of the infection.

DISCUSSION

The rejection under 35 U.S.C. § 103

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if that burden is met, does the burden of

coming forward with evidence or argument shift to the applicant. Id. In order to meet that burden the examiner must provide a reason, based on the prior art, or knowledge generally available in the art as to why it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297 n.24, 227 USPQ 657, 667 n.24 (Fed. Cir. 1985).

On the record before us, the examiner has not met the initial burden of establishing why the prior art relied on would have led one of ordinary skill in this art to arrive at the method of treatment of the rejected claims. While urging that Rodwell describes the generic method for chemically linking an antibody with another molecule and the advantage or benefit for using such conjugates for in vivo delivery to an antigenic site, the examiner acknowledges that "Rodwell does not provide a specific teaching for chemically linking a plurality of antibodies together." (Answer, page 4).

The examiner cites Holder as teaching the production of polyvalent antibodies which recognize multiple epitopes associated with more than one stage of the life cycle of a specific parasite, P. falciparum. However, the examiner acknowledges that Holder does not describe the production of a conjugate comprising a plurality of chemically linked antibodies as presently required by the claims on appeal. (Answer, page 5). The examiner cites Goldenberg ('525) as describing improved methods of disease therapy using cytotoxic agents which can be conjugated to an antibody or antibody fragment which will

bind to markers which are associated with cancer cells in order to enhance their therapeutic effect. (Id.) The examiner relies on Brennan to provide that which is missing from the other three references and urges that Brennan teaches "the technology for chemically linking antibodies together to produce a plurality of antibodies having different antigen binding sites." (Answer, paragraph bridging pages 5-6).

The examiner then concludes (Answer, page 6):

> The benefit of linking antibodies to each other is obvious over Brennan, such that one of ordinary skill in the art would be able to produce a conjugate by chemically linking a plurality (two) of antibodies together to enhance specific and effective targeting of different antigens of the same specie of pathogen (Brennan) which could then be linked to an agent,
> such as a radioisotope or cytotoxic agent for use as a diagnostic or therapeutic agent, as taught by Rodwell and Goldenberg, for the obvious benefit of targeting a plurality of different epitopes of the same specie of pathogen or different antigens expressed at different stages of the life cycle of said pathogen, as taught by Holder. One of ordinary skill in the art would have been motivated to produce such a plurality of chemically linked antibody conjugates to be used in the claimed method of targeting, based on a combination of the cited references, as the benefit for targeting and therapy is exemplified and the claimed method fails to teach any novelty over what the references specifically teach.

What is missing from the examiner's statements in support of this rejection is any reference to facts or evidence which would have directed one of ordinary skill in this art, at the time of the invention, to use the chemically linked antibodies of Brennan in the therapeutic methodology of Rodwell or Goldenberg ('525). As stated by appellants (Reply

Brief, page 5):

> Brennan teaches only a method for making bispecific conjugates of antibody fragments. There is no teaching or suggestion in Brennan of a conjugate comprising a plurality of chemically-linked antibodies or antibody fragments which specifically binds to a plurality of accessible epitopes on a single species of pathogen or of an antigen shed by the pathogen or resulting from the fragmentation or destruction of the pathogen, or of using such a conjugate to target a therapeutic agent to a focus of infection.

As we have stated, in order to establish a prima facie case of obviousness within the meaning of 35 U.S.C. § 103, the prior art must provide a reason or suggestion which would have reasonably directed one skilled in this art to that which is claimed, i.e., the method of targeting a therapeutic agent to a focus of infection using a conjugate comprising a plurality of chemically-linked antibodies which specifically binds to a plurality of accessible epitopes associated with the pathogen which includes a chemically bound therapeutic agent. To the extent that the examiner has established that certain of the components of the claimed invention were known at the time of the invention, the examiner has failed to provide evidence which would have provided a reason or suggestion which would have led one of ordinary skill in this art to combine the various components in a manner to arrive at the claimed invention. The extent to which such reason or suggestion must be explicit in or may be fairly inferred from, the references, is decided on the facts of each case, in light of the prior art and its relationship to the invention. It is impermissible,

however, simply to engage in a hindsight reconstruction of the claimed invention using applicants' specification as a template and selecting elements from references to fill the gaps. In re Gorman,
933 F.2d 982, 986-87, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). Thus, we find that the examiner has not provided the factual evidence which would reasonably support a rejection of the claims on appeal under 35 U.S.C. § 103.

Where, as here, the examiner fails to establish a prima facie case of obviousness, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore the rejection of claims 1, 3-6, 8-10, 19, 20, 24, 25, 39-44, and 46-48 under 35 U.S.C. § 103 is reversed.

Obviousness-type Double Patenting

Claims 1, 3-6, 8-10, 19, 20, 24, 25, 39-44, and 46-48 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-29 of U.S. Patent No. 5,332,567. In setting forth the reasoning in support of this rejection, the examiner recognizes that the claims on appeal are directed to a therapeutic treatment wherein a patient is injected with “an effective amount” of a therapeutic agent while the claims of U.S. Patent No. 5,322,567 are directed to a diagnostic method wherein the patient is injected with “an effective amount” of a diagnostic agent. (Answer, page 7). Without further explanation, the examiner concludes the “the differences fail to provide any

patentable difference in scope. (Id.). Appellants urge that the instant claims are not obvious variations of the claims of the patent. (Reply Brief, page 8). Appellants have focused their arguments on the difference in an effective amount of a therapeutic agent, as required by the appealed claims, as compared with an effective amount of a diagnostic agent as required by the claims of the patent. (Reply Brief, paragraph bridging pages 8-9.)[1] In response the examiner urges that (Supplemental Answer, page 5):

> even though US Patent 5,322,567 is drawn to a diagnostic agent, a therapeutic effect based on an increased concentration of antibody at the target site could additionally provide therapeutic effectiveness, an obvious response to the administration of a diagnostic agent.

What is missing from the examiner's statements in support of this rejection is any reference to evidence or facts which would reasonably suggest that such a modification of the diagnostic methods of the patent claims would have been obvious. Having failed to establish that the claims on appeal are, in fact, obvious over the claims of the patent,

the rejection can not be sustained. Therefore, we reverse the rejection of the claims under the judicially created doctrine of obviousness-type double patenting.

CONCLUSION

[1] Appellants' representative confirmed at the Oral Hearing of November 16, 2000 that a therapeutic effective amount would differ from a diagnostic effective amount both as to type and loading of the agent used in the conjugate required by the claims in question.

The examiner's rejection of claims 1, 3-6, 8-10, 19, 20, 24, 25, 39-44, and 46-48 under 35 U.S.C. § 103 as obvious over the combined teachings of Rodwell, Holder, Goldenberg (‘525), and Brennan is reversed. The rejection of claims 1, 3-6, 8-10, 19, 20, 24, 25, 39-44, and 46-48 under the judicially created doctrine of obviousness-type double patenting is reversed.

REVERSED

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Administrative Patent Judge)
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Carol A. Spiegel) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
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Toni R. Scheiner)
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